L15

L16

0 FILE EMBASE

1 FILE CAPLUS

```
STN search of sequences for:

(ala), cys(gly),

(ala), cys(tyr),
=> e aaaaacg/sqep 5
                    AAAAACCAAA/SOEP
E1
             3
                   AAAAACCQVGCIRKDIARLC/SQEP
E2
              1
              0 --> AAAAACG/SQEP
E3
            1
E4
                    AAAAACYE/SOEP
E5
                    AAAAADAAAAHAAAAAAA/SQEP
             1
=> e aaaaacy/sqep 5
                  AAAAACCAAA/SQEP
             3
                 AAAAACCQVGCIRKDIARLC/SQEP
E2
             1
E3
              0 --> AAAAACY/SQEP
E4
                  AAAAACYE/SQEP
             1
E5
                    AAAAADAAAAHAAAAAAA/SQEP
             1
=> s aaaaacg/sqsp
           123 AAAAACG/SQSP
=> s aaaaacy/sqsp
             8 AAAAACY/SQSP
=> fil medl, biosis, embase, caplus; s frigerio 1?/au; s hadlington j?/au
FILE 'MEDLINE' ENTERED AT 17:02:59 ON 30 MAY 2007
FILE 'BIOSIS' ENTERED AT 17:02:59 ON 30 MAY 2007
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FILE 'EMBASE' ENTERED AT 17:02:59 ON 30 MAY 2007
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FILE 'CAPLUS' ENTERED AT 17:02:59 ON 30 MAY 2007
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
           103 FILE MEDLINE
L_3
L4
            83 FILE BIOSIS
L5
            84 FILE EMBASE
            46 FILE CAPLUS
TOTAL FOR ALL FILES
           316 FRIGERIO L?/AU
L8
             5 FILE MEDLINE
L9
             5 FILE BIOSIS
L10
             2 FILE EMBASE
             8 FILE CAPLUS
TOTAL FOR ALL FILES
L12
            20 HADLINGTON J?/AU
=> s (l1 or l2) and (l7 or l12)
L13
            O FILE MEDLINE
L14
             0 FILE BIOSIS
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TOTAL FOR ALL FILES

L17 1 (L1 OR L2) AND (L7 OR L12)

=> d ibib abs hitseq

L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2004:453253 CAPLUS Full-text

DOCUMENT NUMBER: 141:22183

TITLE: Improved secretion of antibodies from plants

INVENTOR(S): Frigerio, Lorenzo; Hadlington, Jane

PATENT ASSIGNEE(S): University of Warwick, UK SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	KIND		DATE		APPLICATION NO.					DATE									
WO							20040603		WO 2003-GB4983					20031117					
WO	2004046190				A3 20040715														
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,		
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	GE,		
		GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,		
							MA,												
							RO,												
							UG,									- •			
	RW:	BW,														AM.	AZ.		
							ТJ,												
							HU,												
																		TG	
CA									CA 2003-2506505					MR, NE, SN, TD, TG 20031117					
AU									AU 2003-302026										
										EP 2003-811425									
		AT,																	
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										CY, AL, TR, BG, CZ, US 2005-535433									
PRIORITY APPLN. INFO.:										GB 2002-26878									
														Ţ					
OTHER C		MADI	ייזיית	1 4 1 . 4	2210						•								

OTHER SOURCE(S): MARPAT 141:22183

- The authors disclose antibodies containing an Ig heavy chain comprising a $\alpha 3$ domain or a mu domain. The preparation of these antibodies comprises: (a) providing a nucleotide sequence encoding the Ig heavy chain; (b) modifying the nucleotide sequence in the region encoding the C-terminal 18 amino acids of the completed heavy chain to remove, or reduce the effectiveness of, one or more vacuolar targeting sequences; (c) inserting the modified nucleotide sequence into a host cell; and (d) causing the host cell to express the modified nucleotide sequence to form the modified antibody heavy chain and secrete the modified antibody heavy chain from the host cell. This improves the secretion of the antibody from, for example, plant cells. Methods of adding J-chain binding activity to antibodies are also provided. In one example, the improved expression of an IgG containing a $C\alpha 2-C\alpha 3$ domain is demonstrated.
- IT 698349-61-0D, antibody heavy chains-containing
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)

(engineering of antibodies for improved secretion from transgenic plant cells)

10/535433

RN 698349-61-0 CAPLUS

CN L-Tyrosine, L-seryl-L-cysteinyl-L-methionyl-L-valylglycyl-L-histidyl-L-α-glutamyl-L-alanyl-L-leucyl-L-prolyl-L-methionyl-L-asparaginyl-L-phenylalanyl-L-threonyl-L-glutaminyl-L-lysyl-L-threonyl-L-isoleucyl-L-α-α-aspartyl-L-arginyl-L-leucyl-L-serylglycyl-L-lysyl-L-prolyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

PAGE 1-E

IT 698349-36-9

RL: PRP (Properties)

(unclaimed sequence; improved secretion of antibodies from plants)

RN 698349-36-9 CAPLUS

CN L-Tyrosine, L-prolyl-L-alan

SEQ 1 PAAAAACY

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

=> s 17 and 112

L18 2 FILE MEDLINE
L19 2 FILE BIOSIS
L20 2 FILE EMBASE
L21 3 FILE CAPLUS

TOTAL FOR ALL FILES

L22 9 L7 AND L12

=> s 122 not 116

L23 2 FILE MEDLINE
L24 2 FILE BIOSIS
L25 2 FILE EMBASE
L26 2 FILE CAPLUS

TOTAL FOR ALL FILES

L27 8 L22 NOT L16

=> dup rem 127

PROCESSING COMPLETED FOR L27

L28 2 DUP REM L27 (6 DUPLICATES REMOVED)

=> d 1-2 ibib abs

L28 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2003281259 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12808054

TITLE: The C-terminal extension of a hybrid immunoglobulin A/G

heavy chain is responsible for its Golgi-mediated sorting

to the vacuole.

AUTHOR: Hadlington Jane L; Santoro Aniello; Nuttall

James; Denecke Jurgen; Ma Julian K-C; Vitale Alessandro;

Frigerio Lorenzo

CORPORATE SOURCE: Department of Biological Sciences, University of Warwick,

Coventry CV4 7AL, United Kingdom.

SOURCE: Molecular biology of the cell, (2003 Jun) Vol. 14, No. 6,

pp. 2592-602. Electronic Publication: 2003-03-07.

Journal code: 9201390. ISSN: 1059-1524.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200402

ENTRY DATE: Entered STN: 17 Jun 2003

Last Updated on STN: 21 Feb 2004 Entered Medline: 20 Feb 2004

AB We have assessed the ability of the plant secretory pathway to handle the expression of complex heterologous proteins by investigating the fate of a hybrid immunoglobulin A/G in tobacco cells. Although plant cells can express large amounts of the antibody, a relevant proportion is normally lost to vacuolar sorting and degradation. Here we show that the synthesis of high amounts of IgA/G does not impose stress on the plant secretory pathway. Plant cells can assemble antibody chains with high efficiency and vacuolar transport occurs only after the assembled immunoglobulins have traveled through the Golgi complex. We prove that vacuolar delivery of IgA/G depends on the presence of a cryptic sorting signal in the tailpiece of the IgA/G heavy chain. We also show that unassembled light chains are efficiently secreted as monomers by the plant secretory pathway.

L28 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2002711172 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12473100

TITLE: ER-resident chaperone interactions with recombinant

antibodies in transgenic plants.

AUTHOR: Nuttall James; Vine Nicholas; Hadlington Jane L;

Drake Pascal; Frigerio Lorenzo; Ma Julian K-C

CORPORATE SOURCE: Department of Biological Sciences, University of Warwick,

Coventry, UK.

SOURCE: European journal of biochemistry / FEBS, (2002 Dec) Vol.

269, No. 24, pp. 6042-51.

Journal code: 0107600. ISSN: 0014-2956. Germany: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

PUB. COUNTRY:

DOCUMENT TYPE:

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 17 Dec 2002

Last Updated on STN: 7 Mar 2003 Entered Medline: 6 Mar 2003

AΒ In this study, we demonstrate that the folding and assembly of IgG in transgenic tobacco plants is orchestrated by BiP (binding protein), an endoplasmic reticulum resident chaperone. Expression of BiP and calreticulin was examined in transgenic tobacco plants that express immunoglobulin chains, either singly or in combination to form IgG antibody. BiP mRNA expression was lowest in wild-type nontransformed plants and those that expressed immunoglobulin light chain alone. Higher mRNA levels were detected in plants expressing fully assembled immunoglobulin (light and heavy chains), and the most abundant levels of RNA transcript were found in those plants that expressed immunoglobulin heavy chain alone. Estimation of total BiP demonstrated a similar pattern, with the highest levels detected in plants expressing immunoglobulin heavy chain alone. Immunoprecipitation studies demonstrated that BiP was associated with immunoglobulin chains extracted from protoplast lysates, but not from secreted fluids. Again, most BiP was coprecipitated from plants expressing heavy chain only and those that produced full length IgG. The binding of BiP to Ig heavy chains was ATP-sensitive. Co-expression of heavy and light chain resulted in IgG assembly and displacement of BiP from the heavy chain as the amount of light chain increased. Although calreticulin mRNA and total protein levels varied in a similar manner to those of BiP in the transgenic plants, there was no evidence for association between calreticulin and Ig chains, by coimmunoprecipitation. The results indicate that BiP, but not calreticulin, takes part in immunoglobulin folding and assembly in transgenic plants.

=> dis his nofile

```
(FILE 'HOME' ENTERED AT 16:57:08 ON 30 MAY 2007)
     FILE 'REGISTRY' ENTERED AT 16:57:43 ON 30 MAY 2007
               E AAAAACG/SQEP 5
               E AAAAACY/SQEP 5
           123 SEA ABB=ON PLU=ON AAAAACG/SOSP
L1
             8 SEA ABB=ON PLU=ON AAAAACY/SQSP
L2
    FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 17:02:59 ON 30 MAY 2007
L3
           103 SEA ABB=ON PLU=ON FRIGERIO L?/AU
L4
            83 SEA ABB=ON PLU=ON FRIGERIO L?/AU
L5
            84 SEA ABB=ON PLU=ON FRIGERIO L?/AU
L6
            46 SEA ABB=ON PLU=ON FRIGERIO L?/AU
     TOTAL FOR ALL FILES
L7
           316 SEA ABB=ON PLU=ON FRIGERIO L?/AU
L8
             5 SEA ABB=ON PLU=ON HADLINGTON J?/AU
L9
             5 SEA ABB=ON PLU=ON HADLINGTON J?/AU
L10
             2 SEA ABB=ON PLU=ON HADLINGTON J?/AU
             8 SEA ABB=ON PLU=ON HADLINGTON J?/AU
L11
     TOTAL FOR ALL FILES
            20 SEA ABB=ON PLU=ON HADLINGTON J?/AU
L12
L13
             O SEA ABB=ON PLU=ON (L1 OR L2) AND (L3 OR L8 )
L14
             O SEA ABB=ON PLU=ON (L1 OR L2) AND (L4 OR L9 )
L15
             0 SEA ABB=ON PLU=ON (L1 OR L2) AND (L5 OR L10)
             1 SEA ABB=ON PLU=ON (L1 OR L2) AND (L6 OR L11)
    TOTAL FOR ALL FILES
             1 SEA ABB=ON PLU=ON (L1 OR L2) AND (L7 OR L12)
              D IBIB ABS HITSEQ
L18
             2 SEA ABB=ON PLU=ON L3 AND L8
L19
             2 SEA ABB=ON PLU=ON L4 AND L9
L20
             2 SEA ABB=ON PLU=ON L5 AND L10
L21
             3 SEA ABB=ON PLU=ON L6 AND L11
    TOTAL FOR ALL FILES
            9 SEA ABB=ON PLU=ON L7 AND L12
L22
L23
             2 SEA ABB=ON PLU=ON L18 NOT L16
L24
             2 SEA ABB=ON PLU=ON L19 NOT L16
L25
             2 SEA ABB=ON PLU=ON L20 NOT L16
             2 SEA ABB=ON PLU=ON L21 NOT L16
    TOTAL FOR ALL FILES
          8 SEA ABB=ON PLU=ON L22 NOT L16
L27
L28
             2 DUP REM L27 (6 DUPLICATES REMOVED)
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=> log y

STN INTERNATIONAL LOGOFF AT 17:04:08 ON 30 MAY 2007

D 1-2 IBIB ABS